[Second Edition.]

PATENT SPECIFICATION

Application Date : Jan. 17, 1933. No. 1541 / 33. 415,088

Complete Left : Jan. 17, 1934.

Complete Accepted : Aug. 17, 1934.

PROVISIONAL SPECIFICATION.

Improvements in or relating to the Distillation of Liquids Containing Vitamins.

We, THE BRITISH DRUG HOUSES, LIMITED, a British Company, FRANCIS HOWARD CARR and WILLIAM JEWELL, both British subjects, all of Graham Street, City Road, London, N. 1, do hereby declare the nature of this invention to be as follows: —

This invention is for improvements in or relating to the distillation of liquids containing vitamins, particularly oils containing vitamin A, and is more especially concerned with the distillation such as nitrogen or helium.

The temperature used should be as low as is consistent with effective distillation at the pressures employed, and must not in any case be so high as to cause serious destruction of vitamin. For fish liver oils at pressures not above 0.01 mm. temperatures up to about 300° C. may be used with success.

It is an important feature of the preferred method of carrying out our invention that the distance between the

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SPECIFICATION No. 415,088 [Second Edition].

Page 3, line 36, *after* " desired " *insert* " the "
Page 4, line 4, *after* " of " *insert* " an "
Page 4, line 13, *after* " or " *insert* " a "
Page 4, line 42, *for* " distance " *read* " distances "

THE PATENT OFFICE,
14th November, 1936.

According to this invention crude oils containing vitamins are subjected to evaporative fractional distillation in a relatively high vacuum whereby an oil fraction (usually a middle fraction) relatively rich in vitamins, particularly in vitamin A, and relatively free from those constituents which give an objectionable taste or odour to the oils, is obtained.

By " evaporative distillation " we mean the distillation which takes place from the surface of a liquid without ebullition being necessary.

The vacuum employed according to our invention is of the order of a small fraction of a mm. of mercury, and is usually 0.01 mm. to 0.0001 mm. The highest vacua obtainable are preferred since the temperature may then be reduced without unduly decreasing the rate of distillation. If desired, the air may be displaced from the apparatus by means of an inert gas,

[*Price* 1/-].

alcoholysis, to replace glycerol groups by methyl, ethyl or other suitable groups, before treatment according to the invention. It should be noted that when an alcoholysed liver oil is fractionated by evaporative distillation the undesired constituents are usually found in the more volatile fractions, the vitamins being concentrated in the less volatile fractions. The vitamin-containing substance may be subjected to a radiation treatment either before or after treatment according to our invention.

The evaporative fractional distillation may be repeated, if desired, on the several fractions obtained by the application of our invention to any of these materials.

Suitable apparatus comprises an evaporating vessel providing for a large evaporating surface, and a cooled condensing surface sloping in such a manner that the condensate runs down into a collect-

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This invention is for improvements in or relating to the distillation of liquids containing vitamins, particularly oils containing vitamin A, and is more especially concerned with the distillation of fish and animal liver oils.

Certain liver oils, as for example, fish liver oils, in particular those derived from halibut, skipper, dogfish and cod fish, contain a constituent or constituents known as vitamin A, which is required for use in both medicinal and food products. There are present in addition to these valuable substances other constituents of the crude oils which on account of their unpleasant odour and taste considerably limit or entirely prevent the use of the oils in medicinal and food products.

Purification of the oils by ordinary distillation even at reduced pressures results in a loss or total destruction of the vitamins because of the relatively high temperatures necessary and/or oxidation by oxygen present.

According to this invention crude oils containing vitamins are subjected to evaporative fractional distillation in a relatively high vacuum whereby an oil fraction (usually a middle fraction) relatively rich in vitamins, particularly in vitamin A, and relatively free from those constituents which give an objectionable taste or odour to the oils, is obtained.

By "evaporative distillation" we mean the distillation which takes place from the surface of a liquid without ebullition being necessary.

The vacuum employed according to our invention is of the order of a small fraction of a mm. of mercury, and is usually 0.01 mm. to 0.0001 mm. The highest vacua obtainable are preferred since the temperature may then be reduced without unduly decreasing the rate of distillation. If desired, the air may be displaced from the apparatus by means of an inert gas, such as nitrogen or helium.

The temperature used should be as low as is consistent with effective distillation at the pressures employed, and must not in any case be so high as to cause serious destruction of vitamin. For fish liver oils at pressures not above 0.01 mm. temperatures up to about 300° C. may be used with success.

It is an important feature of the preferred method of carrying out our invention that the distance between the evaporating surface and the condensing surface is as small as is practicable, e.g. 0.5 to 1.0 inch, though larger distances may be employed.

Our invention is applicable to any high boiling natural product containing vitamin, particularly to fish liver oils, such as those derived from halibut, skipper, dogfish or codfish. The crude or refined oils may be used, and the process of our invention may be employed in combination with known processes for pretreatment, for purification or for concentration of vitamins. Thus a liver oil may be treated with a saponifying agent, and the unsaponifiable fraction extracted by means of solvents, may be fractionated by evaporative distillation in high vacua. Or the liver oil may first be subjected to alcoholysis, to replace glycerol groups by methyl, ethyl or other suitable groups, before treatment according to the invention. It should be noted that when an alcoholysed liver oil is fractionated by evaporative distillation the undesired constituents are usually found in the more volatile fractions, the vitamins being concentrated in the less volatile fractions. The vitamin-containing substance may be subjected to a radiation treatment either before or after treatment according to our invention.

The evaporative fractional distillation may be repeated, if desired, on the several fractions obtained by the application of our invention to any of these materials.

Suitable apparatus comprises an evaporating vessel providing for a large evaporating surface, and a cooled condensing surface sloping in such a manner that the condensate runs down into a collect-

[*Price* 1/-].

ing vessel which, by any of the known means, may be changed when desired. The condensing surface may be 1 inch above the evaporating surface at one end and 0.5 inch or less at the other. The evaporating vessel is supplied with the necessary heat in any convenient manner. The whole apparatus is exhausted of air, e.g. by means of a suitable pump, to the necessary degree of vacuum.

Our invention is of special value for the production from fish liver oils of fractions rich in vitamin A and free from the greater portion of the substances which impart to the untreated oil those properties which limit its use in medicinal or food products.

The invention is illustrated but not limited by the following examples. The figures in brackets refer to determinations of content of vitamin A by the antimony trichloride test.

EXAMPLE 1.

440 gms. of cod liver oil (500 blue) was fractionated at about 0.001 mm. pressure by evaporative distillation at 282—288° C. In 2½ hours there were obtained 67 gms. of distillate (2,800 blue) and a residue (43 blue); i.e. 15.4% of the oil distilled, carrying 85% of the vitamin content.

EXAMPLE 2.

240 gms. of cod liver oil (240 blue), fractionated at 272—275° C. at about 0.001 mm. pressure gave in 2 hours 32.7 gms. of distillate (2360 blue) and a residue (50 blue); i.e. 9.2% of the oil distilled, carrying 87.5% of the vitamin content.

EXAMPLE 3.

345 gms. of cod liver oil (22 blue), fractionated at 278—280° C. at about 0.001 mm. pressure gave in 2 hours 22 gms. of distillate (460 blue) and a residue (1 blue); i.e. 6.4% of the oil distilled, carrying all the vitamin content.

Dated the 17th day of January, 1933.

THE BRITISH DRUG HOUSES LIMITED,
FRANCIS H. CARR,
WILLIAM JEWELL,
CHARLES ALEX. HILL,
ALAN FRANCIS,
Directors,
E. SIBLEY,
Secretary.

COMPLETE SPECIFICATION.

Improvements in or relating to the Distillation of Liquids Containing Vitamins.

We, THE BRITISH DRUG HOUSES, LIMITED, a British Company, FRANCIS HOWARD CARR, a British Subject, and WILLIAM JEWELL, a British Subject, all of Graham Street, City Road, London, N. 1, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

This invention is for improvements in or relating to the distillation of liquids containing vitamins, particularly oils containing vitamin A, with or without vitamin D, and is more especially concerned with the treatment of fish and animal liver oils.

Certain liver oils, as for example fish liver oils, in particular those derived from halibut, skipper (Scomberesox Saurus), dogfish and codfish, contain a constituent or constituents known as vitamin A and vitamin D which are required singly or combined for use both in medicinal and food products. There are present in addition to these valuable substances other constituents of the crude oils which on account of their unpleasant odour and taste and/or adverse physiological effects considerably limit or entirely prevent the use of the oils in medicinal and food products.

Purification of the oils by ordinary distillation even at reduced pressures results in a heavy loss or even total destruction of both vitamins A and D because of the relatively high temperatures necessary and/or oxidation by oxygen present.

According to this invention crude oils or derivatives thereof containing vitamins are subjected to evaporative vacuum fractional distillation or to molecular fractional distillation in a relatively high vacuum whereby a fraction (usually an intermediate fraction) is obtained, relatively rich in vitamins, particularly in vitamin A, and relatively free from those constituents which give an objectionable taste or odour to the oils. If the crude oil contains in addition to vitamin A vitamin D, a proportion of this vitamin will also be found in the intermediate fractions.

By evaporative vacuum distillation we mean distillation occurring in vacuum under such circumstances that the distilling speed is limited by the rate of creation of vapour from the liquid and

not by the rate of removal of vapour from the vicinity of the liquid. It is to be understood that the evaporative distillation in a high vacuum which takes place in this invention is distinct from the distillation normally associated with ebullition or boiling.

By molecular vacuum distillation we mean distillation occurring under conditions such that a high proportion, in most instances a majority of the molecules which leave the surface do not return to it.

The present process is in general carried out in a high vacuum, as indicated above, and if the vacuum is high enough and the distance between the surfaces is less than the mean free path of the distilling molecules, the process is that known as " molecular distillation ". Our process, is however, not limited to these latter conditions and is in practice an " evaporative " process which may or may not approach true " molecular distillation " according to the conditions of distillation and the nature of the distilling molecules.

The vacuum employed according to our invention is that represented by a pressure of the order of a small fraction of a millimetre of mercury and is usually between 0.01 and 0.0001 mm. The highest vacuum obtainable is preferred since the temperature may then be reduced without unduly decreasing the rate of distillation. If desired, air may first be displaced from the apparatus by means of an inert gas, such as nitrogen or helium.

The temperature used should be as low as is consistent with effective distillation at the pressures employed, and must not in any case be so high as to cause serious destruction of vitamins. For fish liver oils at pressures not above 0.01 mm., temperatures up to 300° C. may be used with success.

It is an important feature of the preferred method of carrying out our invention that the distance between the evaporating surface and the condensing surface should be as small as is practicable, such as 0.5 to 1.0 inch, although variation of these distances is permissible. In every case the square root of the total area of the evaporating and condensing surfaces is great compared with the distance between them.

Our invention is applicable to high-boiling natural products containing vitamins, particularly to fish liver oils, such as those derived from halibut, skipper, dogfish or cod-fish. The crude or refined oils may be used, and the process of our invention may be employed in combination with known processes for pre-treatment, for purification or for concentration of vitamins. Thus a liver oil treated with a saponifying agent, e.g. caustic potash, and the unsaponifiable fraction extracted by means of solvents, may be fractionated by evaporative or molecular distillation in a high vacuum. Or the liver oil may first be subjected to alcoholysis, for example by heating with sodium dissolved in an excess of a suitable alcohol, to replace glyceryl groups by methyl, ethyl, glycol or other suitable groups, before treatment according to the invention.

When an alcoholysed liver oil is fractionated by evaporative distillation, vitamin A is concentrated in the less volatile portions. The vitamin-containing substance may be subjected to an irradiation treatment either before or after treatment according to our invention.

The evaporative and/or molecular fractional distillation may be repeated at the same or at other temperatures if desired on the several fractions obtained by the application of our invention to any of these materials. Suitable apparatus comprises an evaporating vessel providing for a large evaporating surface, and a condensing surface sloping in such a manner that the condensate runs down into a collecting vessel which by any of the known means may be changed when desired. The condensing surface may be 1 inch distant from the evaporating surface at one end and 0.5 inch or less at the other. The evaporating vessel is supplied with the necessary heat in any convenient manner. The whole apparatus is exhausted of air by means of a suitable pump or pumps, to the necessary degree of vacuum. Such an apparatus has been described by C. R. Burch in the Proceedings of the Royal Society " A " Volume 123, page 271 et seq. (March, 1929), but the process is not limited to the use of the distillation apparatus as there described; the size of the pumps and areas and disposition of the evaporating and condensing surfaces may be varied. It is of particular advantage to arrange the heating surface in such a manner that the liquid to be evaporated flows as a continuous film down the surface in such a manner that any unevaporated liquid may be recovered.

For example, an apparatus for our distillation process may be made of glass or of any suitable metals such as copper or nickel or may be part of metal and part of glass or stoneware, and the following description is intended to illustrate the process but not to limit it to the use of such an apparatus.

The apparatus shown in the accompany-

ing drawing consists of a reservoir 11, which may be heated, and which is also provided with a means, e.g. the tube 12 for introducing a current of inert gas such as nitrogen. The material to be treated is melted if not initially liquid, and it is desirable that air present be displaced by passing a current of an inert gas such as nitrogen, and the liquid is allowed to pass into the degassing chamber 13 at the required rate controlled by any convenient method of delivery such as through a pump or needle valve 14. This chamber is connected to a vacuum pump or pumps and may be provided with a means of heating the inflowing liquid, e.g., a jacket 15 having inlet 16 and outlet 17 for heating fluid. The liquid then passes through a seal or trap, such as a U-tube 18 on to the heated surface 19, heat for which may be provided by heated liquids or vapours circulating through pipes 20 and 21 or alternatively by electrical means. This section of the apparatus is exhausted by a pump or pumps to a high degree of vacuum. The lower boiling fraction distils away, is condensed on surface 22 and is led away to a suitable receiver by the tube 23. The residue passes down column 19 through a further trap such as a U-tube 24 into another similarly constructed chamber 25 in which the process is repeated under a high vacuum, employing a higher temperature. The next fraction is distilled from the heated surface 26 and condensed on the surface 27 and led away for collection by tube 28. The residue may then be collected in receiver 29 or if further fractions are desired, another unit or other units may be introduced. It is desirable in each case that the distance between the surfaces of 19 and 22 and between the surfaces of 26 and 27 be less than the mean free path of the distilling molecules. The surfaces of 22 and 27 are kept at a lower temperature than surfaces of 19 and 26 by passing liquid or vapour through the jackets 30 and 31.

The type of distillation described with reference to the drawings may be termed short-path distillation and it is a feature of this invention that an oil-soluble vitamin such as vitamin A may be fractionally distilled by that short path distillation and may also be concentrated thereby.

Our invention is of special value for the production from fish liver oils of fractions rich in vitamin A, and if vitamin D is present in the original oil the fractions will also contain vitamin D, and free from the greater portion of the substances which impart to the untreated oil those properties which limit its use in medicinal or food products.

The invention is illustrated but not limited by the following examples. The figures in brackets in examples 3, 4 and 5 refer to determinations of their content of vitamin A by the Carr-Price test, namely the antimony trichloride test, (Biochemical Journal, 1926, XX. 497).

EXAMPLE 1.

1 part by volume of liver oil is saponified by heating to 60° C. for 40 minutes with 0.84 volume of 95% alcohol, 0.1 volume of water and 0.25 weight/volume of caustic potash. Alcohol is then recovered until about 0.6 volume is obtained, and while still warm the residue is poured into about 10 volumes of warm distilled water and after cooling the unsaponified material is extracted with ether. The ether is then washed several times with distilled water, dried with anhydrous sodium sulphate, filtered and the ether recovered, and the residue may then be distilled in vacuo in the apparatus described.

It may be convenient before distillation to remove most of the cholesterol which is present. This may be effected by dissolving the ether residue in about 5 or 6 volumes of ethyl alcohol, cooling in a freezing mixture to about —10° C. or lower and filtering off the separated cholesterol. The alcohol is then recovered and the residue distilled and if necessary redistilled in a high vacuum by the method described. In this way, using a pressure of the order of 10^{-3} mm. of mercury, there distils at about 140—155° C. a yellowish red oil which contains a very high proportion of vitamins.

EXAMPLE 2.

1 part by weight of liver oil is added to 1 volume/weight of anhydrous methyl alcohol and 0.038 part by weight of sodium metal is added. The mixture is then allowed to stand for 3 hours; two volumes of water are then added and the oil is extracted with ether, washed with water, dried with anhydrous sodium sulphate and the ether recovered. The residue is then subjected to distillation at about 10^{-3} m.m. of mercury. The earliest fractions which distil will contain about 10.5% of the vitamin A, the next 26.4%, and the remainder 53.6%, so that about 79% of the total vitamin A as determined by the antimony trichloride test is contained in about 10% of the material.

EXAMPLE 3.

1 part by weight of cod-liver oil (500 blue) was fractionated at about 0.001 m.m. pressure at 282/288° C., and yielded 0.152 part of distillate (2,800 blue) containing as shown by the antimony trichloride test 85% of the

original vitamin A, the residue being 45 blue.

EXAMPLE 4.

1 part by weight of cod-liver oil (240 blue) was fractionated at about 0.001 m.m. pressure at 272/275° C., and yielded 0.0923 part of distillate at 2360 blue containing as shown by the antimony trichloride test 90% of the vitamin A originally present. The residue was 50 blue.

EXAMPLE 5.

1 part by weight of cod-liver oil (22 blue) was fractionated at about 0.001 m.m. pressure at 278/280° C., and yielded 0.064 part of distillate at 460 blue, showing by the antimony trichloride test that all the vitamin A had distilled in this fraction. The residue gave no appreciable colour reaction with antimony trichloride.

Having now particularly described and ascertained the nature of our said invention, and in what manner the same is to be performed, we declare that what we claim is:—

1. A process for the production of oils rich in vitamins which comprises subjecting vitamin-containing liver oils or derivatives thereof to short-path evaporative distillation in a very high vacuum, e.g. 0.01 to 0.0001 m.m. of mercury.

2. A process as claimed in claim 1 in which the distance between distilling surface and condensing surface is less than the mean free path of the distilling molecules.

3. A process as claimed in claim 1 or claim 2 in which a series of vitamin concentrates is obtained by separate collection of successive fractions of the distillate.

4. A process as claimed in any one of the preceding claims in which the starting material is an alcoholysed or a saponified liver oil.

5. A process as claimed in any one of the preceding claims in which the starting material is a vitamin-containing animal liver oil.

6. A process as claimed in any one of the preceding claims which comprises the steps of removing gas from the liver oil to be fractionated, and subjecting the degassed oil to a continuous process of evaporative vacuum distillation.

7. A process according to any one of the preceding claims in which the liver oil or a fraction obtained therefrom is subjected to an irradiation treatment.

8. Apparatus suitable for the production of oils rich in vitamins by the process of any of the preceding claims, comprising a degassing chamber in which the liver oil is heated in high vacuum to remove dissolved gases, and an evaporating chamber in connection therewith, the evaporating chamber comprising a substantially vertical inner tube capable of being heated electrically or otherwise from the inside and closed at the upper end, the outer surface of the said tube forming the evaporating surface down which the degassed oil may be caused to flow in a thin film, the inner tube being surrounded by a cooled outer tube, the inner surface of which forms the condensing surface, means being provided for feeding degassed oil to the upper end of the inner tube and for separately removing distilled oil and residual oil from the lower end of the outer and inner tubes respectively, the condensing surface being in close proximity to the evaporating surface, means being provided for evacuating the annular space between these surfaces to a high degree of vacuum.

9. Apparatus as claimed in claim 8 comprising a plurality of evaporating chambers, means for collecting separately the distillate from each chamber and for feeding the evaporating surface of each chamber after the first with residual oil from the preceding chamber.

10. Apparatus for the fractionation of liver oils substantially as described with reference to the accompanying diagrammatic drawing.

11. A process for the production of oils rich in vitamins substantially as described with reference to any one of the foregoing examples.

12. Oils rich in vitamins and vitamin concentrates whenever produced by the process of any of the preceding claims.

Dated this 17th day of January, 1934.

E. C. G. CLARKE.

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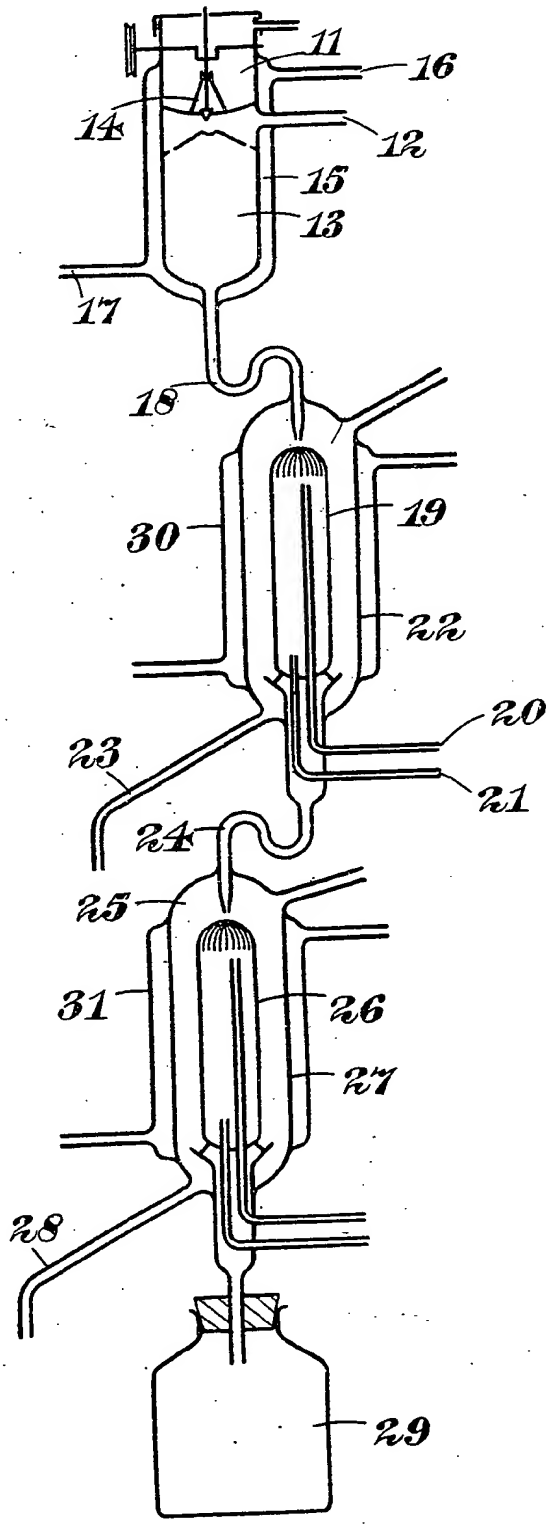
415,088 COMPLETE SPECIFICATION

2nd Edition



[This Drawing is a reproduction of the Original on a reduced scale.]

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